REMARKS

Status of the Claims

Claims 14-37 are pending in the instant application. Claims 1-13 have been canceled. Claims 14, 19, and 25 have been amended for clarity. Claims 20, 34, and 35 have been amended to correct obvious typographical errors. New claim 37 has been added to supply a separate embodiment of the invention.

Amendments to the Specification and Claims

A new paragraph has been inserted before the first line of the specification to set forth the parent applications to which the instant application claims the benefit of priority and to use the preferred language in claiming priority to the parent application.

A new paragraph has been inserted to set forth that this application is related to U.S. Applications 08/510,032 and 08/688,514 and U.S. Provisional Application 60/056,844. This application does not claim priority to these three applications.

On page 9, the paragraph beginning on line 7 has been amended to recite Figs. 3A and B.

On page 13, the paragraph beginning on line 23 has been amended to insert sequence identifiers for the disclosed sequences and to remove the colon in the first sequence which is an obvious typographical error.

On page 15, the paragraph beginning on line 14 has been amended to correct an obvious typographical error. The word "litigation" has been replaced with "ligation."

On page 23, the paragraph beginning on line 8 has been amended to insert sequence identifiers.

On page 24, the paragraph beginning on line 1 has been amended to insert sequence identifiers.

On page 24, the paragraph beginning on line 17 has been amended to insert a sequence identifier and to correct an obvious typographical error.

On page 37, Table 2 has been replaced with a new Table 2 containing sequence identifiers for each disclosed sequences.

Claims 14, 19, and 25 have been amended to replace the term "subject" with "patient" for consistency throughout the claims. The claims have also been amended to provide a separate embodiment of the invention. Support for the amendment can be found on page 60, Example 6.

Claims 20, 34 and 35 have been amended to correct obvious typographical errors.

Support for new claim 37 can be found on page 11, lines 10 and 11.

Objection to the Specification

The specification is objected to because sequence identifiers are not used. Applicants respectfully submit that on May 21, 2002, Applicants filed a paper copy of the Sequence Listing and a Request to Transfer Electronic Copy of Sequence Listing in the parent application, Serial No. 09/506,729, to the present application. The specification has now been amended to recite sequence identifiers. Accordingly, Applicants request withdrawal of the objection.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 14-36 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

Claims 14, 19, and 25 have been amended to recite "that modulates expression of genes in a granulocyte cell population in a patient with a sterile inflammatory disease." Additionally, the term "subject" has been replaced with "patient." Accordingly, the rejection of claims 14-36 is moot.

Claim 13 has been rejected for reciting the phrase "ancillary reagents suitable for use." However, claim 13 has been canceled. Also, original claim 13 does not contain the phrase "ancillary reagents suitable for use."

Rejection Under 35 U.S.C. § 112, First Paragraph

A. Claims 14-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 14-36 as they stand are directed to methods of identifying an agent that modulates expression of genes in a granulocyte cell population found in a patient having a sterile inflammatory disease. The specification describes the claimed method and each of the method steps. Example 6 specifically describes the claimed invention in detail and provides the method

steps for performing the claimed method.

The Office Action states that the written description may be satisfied by a representative number of species by actual reduction to practice, reduction to drawings or by disclosure of relevant identifying characteristics. Applicants respectfully point out that according to MPEP 715.07, actual reduction to practice is not required. For instance, conception of the invention and the filing of the application is sufficient to provide support for the priority of the claimed subject matter (MPEP 715.07, page 700-232). Moreover, as stated in MPEP 2164.02, an applicant need not have actually reduced the invention to practice prior to filing.

The Office Action also states that the skilled artisan would not be able to envision a sufficient number of specific embodiments to describe the broadly claimed genus or combination of genes correlated with an inflammatory disease. Applicants submit that the claims are directed to a method of identifying an agent and not to a product such as an agent, a protein, or a gene. The specification, especially Example 6, provides adequate description of the claimed invention. The specification sets forth each of the steps and the starting reagents required for performing the claimed method.

Given that each of the steps of the claimed method is described in the specification, the specification must convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully request withdrawal of the rejection.

B. Claims 14-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Claims 14-36 as they stand are directed to <u>methods</u> of identifying an agent that modulates expression of genes in a granulocyte cell population found in a patient having a sterile inflammatory disease. An agent that modulates the expression of genes in a granulocyte cell population in a patient is identified in the comparing step of the claimed method. Applicants respectfully point out that the claims are not directed to products such as genes. The present invention is an assay that screens a large number of genes to identify an agent that modulates gene expression associated with sterile inflammatory disease.

The Office Action cites the Wands factors as the test for enablement of an invention.

Regarding the first factor, the "scope/breadth of the claims," the Office Action states that the claims are broad because modulation of the disease can reasonably be dependent on alteration in expression profiles for an enormous number or combination of genes. Applicants respectfully point out that the claims are directed to methods of identifying an agent that modulates the expression of genes in a granulocyte cell population in a patient with sterile inflammatory disease. Each of the steps recited in the claimed methods is described and enabled by the specification. For example, Example 6 specifically provides a method of identifying an agent that modulates the expression of f genes in a granulocyte cell population in a patient with a sterile inflammatory disease. Examples 1-4 describe in detail and enable the steps of isolating a granulocyte population from a patient with a sterile inflammatory disease, treating the granulocyte population with an agent, and preparing a gene expression profile of the granulocyte population. Tables 1 and 2 exemplify gene expression profiles. Example 6 describes in detail and enables the comparing step to identify the agent that modulates the expression of genes. Accordingly, the specification enables the preparation of expression profiles for a large number of genes and comparing the gene expression profiles to identify an agent that modulates the expression of genes in a granulocyte population in a patient. The specification enables the scope and breadth of the claims.

Regarding the second and third factors, "nature of the invention" and "state of the art," the Office Action states that modulating inflammatory diseases via agents that alter expression profiles for a gene or combination of genes is at a comparatively nascent stage of development. Applicants respectfully point out that the claimed invention is directed to methods to identify an agent that modulates the expression of gene(s) in a granulocyte population in a patient with a sterile inflammatory disease. The specification enables the claimed method. The claimed method is not an unpredictable invention given the teachings of the specification for isolating granulocytes, treating granulocytes with an agent, and obtaining and comparing gene expression profiles.

Regarding the fourth factor, "amount of guidance provided," the Office Action states there is insufficient guidance as to what gene or combination of genes would necessarily correlate with modulation of inflammatory diseases. Applicants respectfully point out that the claimed invention is not directed to genes that correlate with modulation of inflammatory

diseases, but to a method of identifying an agent that modulates the expression of gene(s) in a granulocyte cell population in a patient with a sterile inflammatory disease.

Regarding the fifth factor, "number of working examples," the Office Action states that there do not appear to be any substantially relative examples provided. Applicants respectfully point out that Examples 1-6 discloses each of the steps of the claimed method. Example 6 is specifically directed to the claimed invention. There is sufficient guidance from the examples to enable one of ordinary skill in the art to practice the claimed invention without undue experimentation. Further, the court has held that the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice the claimed invention without undue experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

Regarding the sixth factor, "amount of experimentation required," the Office Action states that because of the unpredictability of the art and the lack of working examples, the amount of experimentation that is required is undue. Applicants respectfully point out that the claims as they stand are directed to methods of identifying an agent that modulates the expression of genes in granulocyte cell population in a patient with a sterile inflammatory disease. Each of the steps required for carrying out the claimed invention is adequately described and enabled by the specification. Given the teachings of the specification, it would not require a large amount of experimentation to isolate a granulocyte population, to treat the granulocyte population with an agent, to prepare a gene expression profile of the granulocyte population, and to compare the gene expression profile to identify an agent that modulates the expression of genes in a granulocyte cell population.

In summary, the specification describes the claimed invention in sufficient detail to enable the skilled artisan to make and use the claimed invention. The specification sets forth the required steps for performing the claimed method. The specification provides guidance and example for performing the claimed method. Example 6 specifically discloses the claimed method. Given the guidance and example disclosed by the specification, one skilled in the art would be able to compare gene profiles of granulocyte population from a patient with sterile inflammatory disease, exposed to an agent and unexposed to the same agent, and to identify

agents that modulate the expression of gene(s) associated with sterile inflammatory disease.

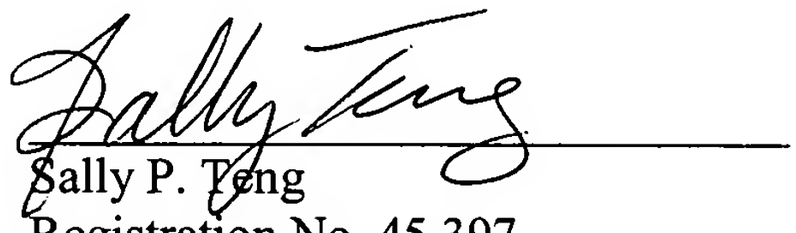
Applicants respectfully request withdrawal of the rejection.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP



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